

REMARKS

I. Status of the Claims

Claims 1-22 were initially filed. Claims 11-22 have been withdrawn and later canceled as the result of a restriction requirement. Claims 1-10 remain pending. The Examiner has indicated the allowability of claims 5, 6, and 9 except for their dependency from a rejected claim.

II. Claim Rejections

A. 35 U.S.C. §102

The Examiner has sustained the rejection of claims 1-4 and 10 under 35 U.S.C. §102(a) for alleged anticipation by Rieger *et al.*, in spite of the submission of a Rule 131 declaration by the inventors (submitted August 3, 2004) to antedate the reference. Specifically, the Examiner asserted that the declaration is insufficient because of two reasons: first, the accompanying evidence does not show contemplation of the claimed screening process; and second, the cited reference discloses cytokines and lipopolysaccharide (LPS) as NOS2 modulators, whereas the submitted evidence shows experiments using aminoguanidine (AG) as a NOS2 inhibitor. Applicants respectfully disagree with the Examiner, particularly in light of the concurrently filed supplemental declaration pursuant to 37 C.F.R. §1.131.

Regarding the contemplation of the claimed screening process, inventors of this application, Drs. Stefan Ambs and Curtis C. Harris, state in their supplemental declaration that the conception and completion of the claimed screening process took place at the same time when the underlying invention was first made, because the conception and completion of the claimed invention are naturally and logically associated with the experiments shown in the evidence accompanying the Rule 131 declaration of August 3, 2004 (paragraph 3 of the supplemental declaration). The inventors further attest that "the use of p53-deficient cells to screen for NOS2 modulators was simultaneously conceived and completed when the substantive invention was made. The use of p53-deficient cells for screening purpose is an integral part and

a logical permutation of the invention in evidence. Because the invention in evidence indicates a growth-promoting effect by NOS2 in p53-deficient tumor cells that can be reversed by an inhibitor of NOS2, one of ordinary skill in the art would therefore immediately recognize that p53-deficient cells can be used for the identification of NOS2 modulators. Also, because the very same assay system as shown in the evidence can be used for this screening process, the invention as presently claimed was not only conceived but also completed prior to November 5, 1998." (paragraph of 4 of the supplemental declaration)

Regarding the different identity of NOS2 modulators disclosed in the Rieger *et al.* reference and in the evidence submitted with the declaration of August 3, 2004, Applicants contend that the identity of NOS2 modulators has no bearing on the scope of the claimed invention, which is the method for identifying such modulators. Unlike a method for use of NOS2 modulators, a screening method as defined by the pending claims of this application is applicable to the identification of all potential modulators of NOS2, regardless of their identity or whether they have been named in the specification.

Even if the claimed subject matter in this application were the use of NOS2 modulators, and the species of NOS2 modulators were relevant to the claim scope, Applicants contend that by submitting evidence of reduction to practice using one species of NOS2 inhibitor, the August 3, 2004, declaration would nonetheless effectively antedate the Rieger reference, which relates to other species of NOS2 modulators. The relevant sections of the MPEP state that,

[A] 37 CFR 1.131 affidavit is not insufficient merely because it does not show the identical disclosure of the reference(s) or the identical subject matter involved in the activity relied upon. If the affidavit contains facts showing a completion of the invention commensurate with the extent of the invention as claimed is shown in the reference or activity, the affidavit or declaration is sufficient, whether or not it is a showing of the identical disclosure of the reference of the identical subject matter involved in the activity.

... ..

Proof of prior completion of a species different from the species of the reference or activity will be sufficient to overcome a reference indirectly under 37 CFR §1.131 if the species shown in the reference or activity would have been obvious in view of the species shown to have been made by the applicant ... Alternatively, if the applicant cannot show possession of the species of the reference or activity in this manner, the applicant may be able to antedate the reference or activity indirectly by, for example, showing prior completion of one or more species which put him or her in possession of the claimed genus prior to the reference's or activity's date. The test is whether the species completed by applicant prior to the reference date or the activity's date provided an adequate basis for inferring that the invention has generic applicability. ...

(MPEP §715.02 and §715.03. Emphasis added)

Taken together, these two sections of the MPEP do not impose a strict requirement for a Rule 131 declaration to demonstrate possession of the exact same subject matter as that disclosed in a cited reference, as §715.02 states that a declaration "is not insufficient merely because it does not show the identical disclosure of the reference(s)"; rather, the requirement is a showing of "an adequate basis for inferring that the invention has generic applicability" (see §715.03).

As Drs. Ambs and Harris attest in the supplemental declaration, it would be obvious for one of skill in the art to regulate tumor growth in p53-deficient cells using any NOS2 modulator, in light of NOS2's effect on p53-deficient tumor cell growth illustrated by the present application (paragraph 3 of the supplemental declaration). This is because, according to the inventors, "[a]lthough this invention is based on the observation that one particular NOS2 inhibitor, aminoguanidine (AG), can reverse the growth-promoting effect of NOS2 in p53-deficient cells, the general mechanism of regulating NOS2's effect on tumor growth in p53-deficient cells, as illustrated by this observation, is applicable to any and all NOS2 modulators. Thus, when the use of NOS2 modulators is concerned, the use of NOS2 modulators beyond the exemplary species used this application would be obvious to one of skill in the art." (paragraph 5 of the supplemental declaration) Applicants hence contend that the antedating invention as evidenced by the August 3, 2004, declaration provides a reasonable inference that the invention

has generic applicability to all NOS2 modulators for their use in controlling p53-deficient tumor growth. The use of additional NOS2 modulators not named in the evidence would be obvious to a skilled artisan in view of the general mechanism of action. Therefore, the evidence provided by the Rule 131 declaration of August 3, 2004, would sufficiently antedate the Rieger *et al.* reference according to the standards of MPEP §715.02 and §715.03.

In summary, it is established by inventors' supplemental declaration that the conception and completion of the claimed screening method took place at the same time when the invention, shown in the evidence accompanying the Rule 131 declaration submitted August 3, 2004, was completed, because the screening method is an integral part and a logical permutation of the invention, and would be immediately recognized by one of skill in the art upon understanding the invention. Because the invention as defined by the pending claims is a screening method, Applicants do not believe that the identity of NOS2 modulator species has any relevance to swearing behind the Rieger *et al.* reference. If, however, the modulator species were deemed relevant, Applicants contend that the evidence shown in the Rule 131 declaration of August 3, 2004, would still sufficiently antedate the Rieger *et al.* reference under the MPEP standards, as the inventions have established in the supplemental declaration the generic applicability of the invention and the obviousness of using unnamed NOS2 modulators to control the growth of tumor cells lacking functional p53. Thus, the Rieger *et al.* reference is not available as a §102(a) prior art reference and the anticipation rejection should be properly withdrawn.

B. 35 U.S.C. §103

The Examiner further sustained the rejection of claim 8 under 35 U.S.C. §103(a) for alleged obviousness over the Rieger *et al.* reference. In light of the supplemental Rule 131 declaration and the discussion in the last section, Applicants submit that Rieger *et al.* is properly antedated and therefore not available as a prior art reference. Accordingly, there lacks an adequate basis for an obviousness rejection. The withdrawal of the obviousness rejection is respectfully requested.

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Amdt. dated December 13, 2004
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Examining Group 1642

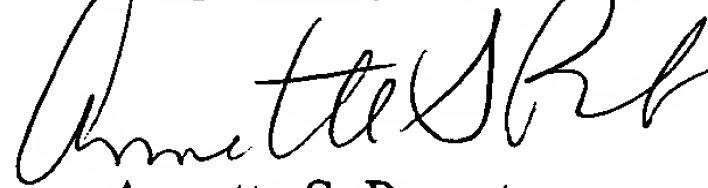
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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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